

Chicago. May 10, 1983

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## I Introduction

1. Purpose - To emphasize importance of "sense of need" in regulating types of DNA modifications that serve to regulate actions of genes -- individually and during development.
2. My involvement - start late 1920s - to 1931:
  - ① my entry - genetics - 1921. where, why, state of discipline
  - ② 1900 - 1921.
  - ③ 1914 - 1921 - *Drosophila* - Marquardt - Slide 1. Eano.
  - ④ 1921 - Marquardt - no esp. Cytology - Cornell Woods to Cornell
  - ⑤ Ph.D. thesis - find - consequence
  - ⑥ 1928-29 - pachytene Chr. 5 Slide 2 - pachytene. Translocation
  - ⑦ 1928 - X-ray mutants. Chr. rearrangements. Harrow. Thysano
  - ⑧ Stadler - 1928-30 - X-ray. mutants. Losses of genes.
  - ⑨ My interest - linkage group + chromosomes
3. summer 1931 - Marquardt - X-ray pollen summer 1930
  - ① Seed from ♀ standard recessive allele × ♂ Dom. allele. esp. Expect - recombination - F1 esp. loss of Dom.
  - ② Grow seed 1931. Watch for plants with recessive alleles
  - ③ Estimate chromosomes of plants - pachytene - give - Purdy etc.
  - ④ Results - excellent. Much new.
4. Fall 1931 - Reprint Berkeley - Fraen - has normally - diploid recessive in normal chr.
  - ① My response = very obs. Reason: not reported: Must be unstable: water of a and its change
  - ② Observed  $2 \times 2$   $\begin{array}{c|c} 1 & 2 \\ \hline 1 & 1 \\ 2 & 4 \end{array}$  <sup>mut</sup> true - junction
  - ③ mutation = 0
  - ④ Response - Berkeley.
  - ⑤ Letter to Stadler - For summer 1932. Select var. plants, NOT translocated or broken 1931 but all new.
5. Summer 1932 - <sup>C to 1932 - 1933</sup>
  - ① Rec. others - all var. plants
  - ② Reinterpretation of my obs. Slide 3.
  - ③ Speed of fusion - sensing

6. same time - Homo s-c translocation  
centromere location - change  
 ① c. <sup>micro</sup> - centromere to nucleolus organizer - diplotene breakdown, job  
 ② Break & fusion - at nucleolus. Bridge at R.I.  
 ③ question - what later? single broken end entering nucleus

## II. Beginning of study of 6.f.b. cycles 1936-37

1. TO examine - see para centric inversions - 6.f.b. stages.  
Cross over meiotic profiles - dicentric ch.acentric fragments.
2. Consequence = Slide 4. Diagram. Slide 5-7, Photo
3. Next division - Microspore (to Pollen grain).  
Replication - fusion of chromatids apposing broken ends.

## III. For following mirror - Behaviour of broken ends

1. set-up. To obtain functioning pollen: full germination - carrying broken end in each sperm Slide 8 Diagram
2. Pollen + egg development from a pollen.

Slides 9-10, Photo.  
Pollen dev. <sup>10%</sup> Embryo-embryo. <sup>10%</sup> embryo  
Unif. rec. expt. Fusion - double fertilization - sister organ - endosp.

3. The test - surprise. Endosperm - Embryo.  
In embryo - healing, many test. New telomere found  
stable telomeres.  
(+) Mutant - no healing in plant - 6.f.b. cyc. all mirror  
A programmed repair complex operating in plant -  
not in endosperm: dead end DNA?
4. Paracentric - Ring ch. = fusions of ch. No healing. <sup>\* rare</sup>  
\* Early fusion before replication, no telomere found or  
single broken end - replication required for  
fusion in gamete flight & endosperm.  
Healing - telomere formation during replication?

IV. The set-up to test fusion of broken DNA in embryo -  
<sup>(3)</sup>  
same as above but. ♀ gamete + ♂ gamete - both

Fusion? Healing? = 1938-39. Pub. 1940 PRC  
Result. Slide 11. Diagram.

Healing = sequence-

a) Ring ds = rare sister strand exchange. Random  
b) b. \* b. <sup>2 way</sup> <sub>any</sub> cell possible - healing selected

V. The hypothesis - 1942 - large scale b. \* b. Mitochondria

1. 450 b. \* b. kernels - summer 1942.

2. germination? - Surprises - Before healing = bricks.  
Genome change: out + in. adjacent cells, different  
genomes.

3. The significance of side branches - slivers

4. Plants. (2). Ctp. like F<sub>1</sub>. Kernels & plant =  
could show mutants - regeneration - phenotypes

5. The seedling test - branch - 40 kernels - from ear  
ear. winter 1944-45

6. The result - Starting. Chlorophyll genes - patterns  
of expression.

7. Transplants - changes in patterns - turn  
sectors?

8. Conclusion -  
single event - mitosis - one cell gained what other  
cell lost. what each = controlled gene + previous  
many cell generations later.

De formation event -- cell heredity - later explicit

9. Conclusion - find out. Basic mechanism of  
regulation of gene action clearly. etc.

→ [No DNA as genetic material recognized until 1947.]

VI. Discovery of transposable gene-control elements 1947/48

1. Origins - activation, previously silent elements
2. Relation to previous experience - Rhoeder -  $\alpha_1$  - Dotted history in  $\alpha_1$ : mutant, brown, not purple at 1914 - genes (b) - stability, (c) Rhoeder - mid 1930s.  $\text{DT}^+$  genes  
 (a) Osborne - Anthocyanin dots elsewhere - purple.  
 (d) Germinal mutant - stable. Difference: poly,  $A^{N_1}(P_1)$ ,  $A^{N_2}(P_2)$  form polytypic changes in dev. regulation of action genes
3. Decision - make DT appear - b-g Cycle - same technique  
 meadow - bridge - bush - spore DNA 1. gen. meadow - 0.022  
 pollen, 2 options:
  - (a) First test - any time during cycle. Slide 13
  - (b) Dot branching - same result:  $\geq 3$  independent activation sites - By necessity - 1st ch. in spore = 2nd bridge.  
 Screening =  $\alpha_1$  meadow + purple fruit.
4. How increasing number of transposable element recognized: each independent of others.  
 Re-D; D-a; Spm, Em, Mu, Ub, Bgl, Fca, Mut,  
 assoc. with various effects - etc. more than 10 more.

VII. Examples of modifications of action of genes. Biochemical

1. Reat Adh - (no Ac) = 402; 11 bp <sup>mutant</sup>; 8 bp. hot due to <sup>not</sup>  
 " " + Ac = some reversions: clean removal. 8 bp. revision  
 $\text{not}$  significant for changed regulation.
2. Lz-mt - Dc - Ac system: Phenotypes. Color fan. Slide 14.  
 no Ac - enzyme - Turner. with Ac - 12 turns. to normal.  
 $\leftarrow$ ,  $\rightarrow$  reaction.  
 $\leftarrow$ ,  $\rightarrow$  reaction.
3. lgl-m13 - Spm system:  
 no Spm - enzyme = Right enzyme - wrong turn. CBM - muscle turn  
 Spm - colorless - mutation - germinal - reversion

4. Mut into PTH. 1-35 insert. other 70% - larger. (5)  
mutation - changed degree of enzyme activity.
5. DnatSh1 - complex. inserts into Ds. displacing  
large segment of inserted. same b.p. contribution  
at end + distance as Dnat PTH.
6. Origin receptor from initial insert.

$\text{P}_{\text{thy}}^{\text{mut}} \rightarrow \text{D}_{\text{thy}}^{\text{mut}} = 4\%$ . loss of control  
in hundred b.p.

### VII Types of gene regulation associated with inserts and their modifications in 1970

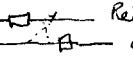
1. Control of products of regulators -  $\beta$ -gal, SV40, bZ, etc.  
  - ① all have "trans-activating" activity - tumor, if, - programmed.
  - ② Some have other products - inhibitors, suppressors, pattern regulators - these products - programmed.
 independent programming for each product - Examples -
  - i) Receptor at gene locus - low level gene action. Regulator: SV40 turn off gene action - no base pair substitution - tumor or organ
  - Pattern of gene expression in diff. tissues as "compartments"
  - ii) Receptor at gene locus - no gene action. Regulator: active product - trans-activating, turns on gene action. Cycles off on-off programmed at RpdB or
2. Change in "receptor" - changed time of response to trans-acting  
product of regulator. states
3. Programming events - no change in nucleotide sequence: co-programming  
sequences - cell heredity of each - epigenetic
4. Non-clonal patterns: (Clytra, Lady bird beetles; plant leaf patterns),  
many flower patterns, element at 8 kb - can regulate this.
5. Most significant - flowering plants - programming + erasure -  
  - (i) Reason. Requirements of the system illustrated by inserts -

- (c) Exceptionally clear example by one state of terrain -  
 Remarkable patterns of gene expression - sequence of  
 programming events with cell hierarchy of plant tissues.  
 (like morphogenesis, no b.p. change) autonomy. Final  
 expression following final reprogramming.  
 Flower pattern -- similar requirements for genes.

(d) Insecticidal resistance - Examples:

- ① Tissue with Zygote
  - ② At other times = permeabilization R locus.  
 (Known from "presettling")
  - ③ Rare but predictable. ReptP  
 $P = \text{pericarp} + \text{Cdr. Antithymic}$   
 $\text{RxP} = \text{Uterus. Sclerites} + \text{ect. structures}$   
 Presetting pattern - Bm 11/11
- Pericarp vs aleurone layers. Slide 15 Color
- ReptP -- Preset pattern-sector. Slide 16-18 Color  
 Sector - event-cell hierarchy -  
 progeny - cleared.

IX Locations of insects - Detection -

1. Initially: Cross borders -  Return to weed type'
2. Roots -  $n_1 m_1$ ; hyphae, others  $a_1 m_1 s_1 / a_2 m_2 \rightarrow R_{12}$
3. Particularly instruction in roots -  $n_1 \rightarrow t - c_1$  Slide 19

## Studies

1. Ears Monodelphid.
2. Paclt Tens - maize
3. Diagram - Ring chr. behavior
4. " - Hetero. endosperm + L. C.O. Correspond?
5. Photo - Bridges PI, TI
6. " - " Pro II, P II, Early T II
7. " " T II later
8. Diagram - Dif chg / normal. C.O. Bridge. Fusion
9. Photo - whole kernel - embryo - Endosperm areas.
10. " - Long. section - 2 halves. " + embryo areas
11. Diagram. G. or x b. g = Dicentrics - bridges.
12. Photo - T II bridge. Same as slide?
13. Photo - 2 rows of kernel - DZ-O<sub>r</sub>
14. Ear. Colr - I Sh B<sub>3</sub> - C abg - Phenotype
15. Colr. Commercial maize
- 16, 17, 18 Colr. Re P
19. Kernel - N<sub>f</sub>; st; N<sub>f</sub>/st; C.O.S.